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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,664	09/19/2005	Christophe de Romeuf	065691-0389	5235

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FOLEY AND LARDNER LLP  
SUITE 500  
3000 K STREET NW  
WASHINGTON, DC 20007

EXAMINER
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DAHLE, CHUN WU

ART UNIT	PAPER NUMBER
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1644

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04/09/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/527,664	<b>Applicant(s)</b> DE ROMEU ET AL.	
	<b>Examiner</b> CHUN DAHLE	<b>Art Unit</b> 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01/16/2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1, 2 and 22-45 is/are pending in the application.
- 4a) Of the above claim(s) 30 and 34-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 22-29, 31-33, and 38-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

1. Applicant's amendment to the claims, filed on January 16, 2009, is acknowledged.

Claims 3-21 have been previously canceled.

Claims 43-45 have been added.

Claims 1, 2, and 22-45 are pending.

Claims 30 and 34-37 stand withdrawn from further consideration under 37 C.F.R.

1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 28, 2008.

Claims 1, 2, 22-29, 31-33, 38-42 and newly added claims 43-45 are currently under consideration as they read on the elected species of an anti-HLA-DR antibody.

2. This Office Action will be in response to applicant's arguments, filed on January 16, 2009.

The rejections of record can be found in the previous Office Action, mailed on July 22, 2008.

3. Applicant's remarks regarding the non-considered foreign references and NPL references on IDS (filed on March 11, 2005) are acknowledged (the references have not been considered because no copies have been provided, see Office Action mailed on July 22, 2008 for detailed explanation). Applicant asserts that the copies of those references should have been provided directly by WIPO. Further, applicant asserts that the missing documents are submitted with the Remarks filed on January 16, 2009.

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However, no records show that said references have been provided by either WIPO or applicant. Therefore, the foreign documents and NPL references, cited on IDS filed on March 11, 2005, have not been considered.

4. Applicant's amendment to the specification has been entered. In light of the amendment, the prior objection to the specification for the use of trademarks has been withdrawn.

5. In view of applicant's amendment to the claims, the prior objections to the claims have been withdrawn.

6. In light of applicant's amendment to the claims, the prior rejections, under 35 U.S.C. 112, second paragraph, have been withdrawn.

7. Upon reconsideration, the prior rejection (against claim 32) under 35 U.S.C. 112, first paragraph, written description, new matter, has been withdrawn.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 2, 22-29, 38-42, and newly added claims 43-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Beliard et al. (WO 01/77181) as evidenced by Beliard et al. (US Patent Application US 2003/0175969) for reasons of record.

The previous Office Action, mailed on July 22, 2008, states:

*"It is noted that Beliard et al. (WO 01/77181) is in French. However, given that Beliard et al. (US Patent Application US 2003/0175969) is the national stage under 35 U.S.C. 371 of PCT international application PCT/FR01/01127 that is published as Beliard et al. (WO 01/77181), Beliard et al. (US Patent Application US*

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2003/0175969) is deemed to be the English translation of *Beliard et al.* (WO 01/77181). Thus, the rejection is based on the content of *Beliard et al.* (US Patent Application US 2003/0175969).

*Beliard et al.* teach human anti-Rhesus D monoclonal antibody made in rat myeloma host cell YB2/0 that has particular glycosylation profile in the Fc region wherein said human anti-Rhesus D monoclonal antibody exhibits enhanced CD16 mediated ADCC function compared to commercially available homologous antibodies (e.g. see Examples 1-3 on pages 6-17).

Given that the prior art human anti-Rhesus D monoclonal antibody is made in the same YB2/0 host cells as the claimed antibody, the prior art antibody would inherently have the properties, e.g. an ADCC rate of greater than 100% at a concentration of 10/ng/ml or less, induction of cytokines such as interleukine or TNFs by Jurkat CD16 cells or CD16 expressing effector cells of the immune system. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not have the properties as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980)."

Applicant's arguments, filed on January 16, 2009, have been fully considered but have not been found persuasive.

Applicant argues that the instant invention differs from the prior art in that the instant invention encompasses additional step of selection of antibody for its affinity to CD16 and its ability of induction of cytokine production. Applicant argues that the reference does not teach this selection step and thus has very low probability of arriving at the claimed antibody being able to induce a rate of production of at least one cytokine by the Jurkat CD16 cells or a CD16 receptor-expression effector cell of the immune system of greater than 60%, compared with the same antibody produced in a CHO line or with a commercially available homologous antibody.

This is not found persuasive for following reasons:

In contrast to applicant's assertion, the specification clearly teaches that antibodies produced in YB2/0 cells induce strong ADCC activity and the production of cytokines (e.g. see Example 7). Applicant's own specification discloses that the prior art antibody, anti-Rh D

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antibody from Beliard et al. (WO 01/77181), was made from YB2/0 cells and states that the prior art antibody exhibits modified glycosylation in the constant region of the antibody resulting in improvement of ADCC activity (e.g. see pages 2-3). Thus, the prior art antibody inherently has the ability to induce a rate of production of at least one cytokine by the Jurkat CD16 cell or a CD16-expressing effector cell of the immune system of greater than 60% compared with the same antibody produced in a CHO line or with commercially available homologous antibody. Applicant has not provided any objective evidence to show that the prior art antibody produced in the same host cell YB2/0 as the instant claimed antibody would not meet the claimed functional limitations. Therefore, applicant's arguments have not been found persuasive.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 31-33, and newly added claim 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tso et al. (US Patent 6,894,149, of record) in view of Ogawa et al. (EP 1229125, published on July 8, 2002, of record) for reasons of record.

The Office Action, mailed on July 22, 2008 states:

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*“Tso et al. teach a method for treating diseases such as chronic myeloid leukemia by administering humanized anti-HLA-DR monoclonal antibody (e.g. see columns 4 and 7-8). Tso et al. further provided methods of genetically engineering of the anti-HLA-DR antibodies and working examples of method of making anti-HLA-DR antibodies using conventional hybridoma techniques (e.g. see columns 6 and 14).*

*The reference teachings differ from the claimed invention by not describing humanized anti-HLA-DR antibody made in rat myeloma YB2/0 cells.*

*Ogawa et al. teaches that antibodies e.g. humanized antibodies, made in YB2/0 host cells, have a higher antibody-dependent cell-mediated cytotoxic activity (ADCC) and are useful as a pharmaceutical agents for treating diseases such as cancer (see entire document, particularly columns 3-5). Ogawa et al. teach that cDNA encoding antibodies can be cloned from known hybridomas and expressed in YB2/0 cells and the antibodies can be produced in serum free environment (e.g. see column 5).*

*Given the availability of the hybridomas producing anti-HLA-DR antibodies together with general immunoglobulin gene cloning and expression strategies, it would have been a matter of routine experimentation well within the ordinary skill level of art to make humanized anti-HLA-DR antibodies in rat myeloma cell YB2/0. Additionally, such humanized anti-HLA-DR antibodies made in rat myeloma cell YB2/0 would inherently have the properties of an ADCC rate of greater than 100% at a concentration of 10ng/ml or less and a rate of IL-2 production by a CD16 expressing effector cell of the immune system of greater than up to 1000% at a concentration of 10hg/ml or less compared with the same antibody expressed in CHO cell line.*

*One of ordinary skill in the art would have been motivated to make humanized anti-HLA-DR antibodies taught by Tso et al. in YB2/0 cells for enhanced ADCC function for therapeutic regimens in humans in view of the teachings from Ogawa et al. of the advantage of producing antibodies in YB2/0 cells. One of ordinary skill in the art would have had a reasonable expectation of success in generating humanized anti-HLA-DR antibodies in YB2/0 cells and used said antibodies in a method of treating chronic myelocytic leukemia. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.”*

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant argues that Tso et al. do not teach an antibody that have the ability to induce a rate of production of at least one cytokine by Jurkat CD16 cells or a CD16 receptor-expressing effector cell of the immune system of greater than 60%, compared with the same antibody produced in a CHO line or with a commercially available homologous antibody. Applicant argues that Ogawa et al. do not teach the claimed limitation. Applicant argues that at the best a possibility that the claimed limitation would met; therefore, reliance on inherency is not appropriate.

This is not found persuasive for following reasons:

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Attorney argument, absent supporting evidence, is entitled to little, if any, weight. *Velander v. Garner*, 348 F.3d 1359, 1371, (Fed. Cir. 2003); *Meitzner v. Mindick*, 549 F.2d 775, 782, (CCPA 1977). Further, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. See MPEP 2112.

In this case, applicant has not provided any objective evidence to show that the prior art antibody that is made in the same manner as the instant antibody would not have the intrinsic ability to "induce a rate of production of at least one cytokine by the Jarkat CD16 cell or a CD16 receptor-expressing effector cell of the immune system of greater than 60%, compared with the same antibody produced in CHO line or with a commercially available homologous antibody". Such claimed limitation would be intrinsic characteristics of the prior art antibody made in YB2/0 host cells. Applicant's own Examples disclosed in the specification demonstrate that antibodies made in YB2/0 host cells, e.g. anti-HLA-DR antibody, anti-Rh D antibody, anti-CD20 antibody, all show the above recited limitation. Given that the combined teachings of Tso et al. and Ogawa et al. would render it obvious for antibodies made from YB2/0 cells because YB2/0 produced antibodies exhibits enhanced ADCC activity, the recited limitation of ability to "induce a rate of production of at least one cytokine by the Jarkat CD16 cell or a CD16 receptor-expressing effector cell of the immune system of greater than 60%, compared with the same antibody produced in CHO line or with a commercially available homologous antibody" is a necessary feature of the prior art antibody even if it was unknown at the time of the prior invention.

Therefore, applicant's arguments have not been found persuasive.

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined

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application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1, 2, 22-29, 31-33, 38-42, and newly added claims 43-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 64-80, 86, 88, 90-93 of copending USSN 10/551,819, claims 18, 19, and 21 of copending USSN 10/575,218, and claims 19-38 of copending USSN 11/039,877 for reasons of record.

Applicant requests that the provisional double patenting rejection be held in abeyance until allowable subject matter has been.

Given that no terminal disclaimer signed by the assignee and fully complied with 37 CFR 3.73(b) was filed, the provisional obviousness-type double patenting rejection is maintained.

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15. Conclusion: no claim is allowed.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Eileen O'Hara can be reached 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

April 6, 2009

Chun Dahle  
Patent Examiner  
TC 1600

/Maher M. Haddad/  
Primary Examiner,  
Art Unit 1644